FOXG1 syndrome

FOXG1 syndrome is a condition characterized by impaired development and structural brain abnormalities. Affected infants are small at birth, and their heads grow more slowly than normal, leading to an unusually small head size (microcephaly) by early childhood. The condition is associated with a particular pattern of brain malformations that includes a thin or underdeveloped connection between the right and left halves of the brain (a structure called the corpus callosum), reduced folds and grooves (gyri) on the surface of the brain, and a smaller than usual amount of brain tissue known as white matter.

FOXG1 syndrome affects most aspects of development, and children with the condition typically have severe intellectual disability. Abnormal or involuntary movements, such as jerking movements of the arms and legs and repeated hand motions, are common, and most affected children do not learn to sit or walk without assistance. Babies and young children with *FOXG1* syndrome often have feeding problems, sleep disturbances, seizures, irritability, and excessive crying. The condition is also characterized by limited communication and social interaction, including poor eye contact and a near absence of speech and language skills. Because of these social impairments, *FOXG1* syndrome is classified as an autism spectrum disorder.

FOXG1 syndrome was previously described as a congenital variant of Rett syndrome, which is a similar disorder of brain development. Both disorders are characterized by impaired development, intellectual disability, and problems with communication and language. However, Rett syndrome is diagnosed almost exclusively in females, while *FOXG1* syndrome affects both males and females. Rett syndrome also involves a period of apparently normal early development that does not occur in *FOXG1* syndrome. Because of these differences, physicians and researchers now usually consider *FOXG1* syndrome to be distinct from Rett syndrome.

Frequency

More than 100 cases of this rare condition have been reported.

Genetic Changes

As its name suggests, *FOXG1* syndrome is caused by changes involving the *FOXG1* gene. This gene provides instructions for making a protein called forkhead box G1. This protein plays an important role in brain development before birth, particularly in a region of the embryonic brain known as the telencephalon. The telencephalon ultimately develops into several critical structures, including the the largest part of

the brain (the cerebrum), which controls most voluntary activity, language, sensory perception, learning, and memory.

In some cases, *FOXG1* syndrome is caused by mutations within the *FOXG1* gene itself. In others, the condition results from a deletion of genetic material from a region of the long (q) arm of chromosome 14 that includes the *FOXG1* gene. All of these genetic changes prevent the production of forkhead box G1 or impair the protein's function. A shortage of functional forkhead box G1 disrupts normal brain development starting before birth, which appears to underlie the structural brain abnormalities and severe developmental problems characteristic of *FOXG1* syndrome.

Inheritance Pattern

FOXG1 syndrome is considered an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder. All reported cases have resulted from new mutations or deletions involving the *FOXG1* gene and have occurred in people with no history of the disorder in their family. Because the condition is so severe, no one with *FOXG1* syndrome has been known to have children.

Other Names for This Condition

- FOXG1-related disorder

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Rett syndrome, congenital variant
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3150705/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html
- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html
- Health Topic: Speech and Communication Disorders
  https://medlineplus.gov/speechandcommunicationdisorders.html

Genetic and Rare Diseases Information Center

- FOXG1 syndrome
  https://rarediseases.info.nih.gov/diseases/12825/foxg1-syndrome

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: Intellectual and Developmental Disabilities
  https://www.nichd.nih.gov/health/topics/idds/Pages/default.aspx
- National Institute of Neurological Disorders and Stroke: Microcephaly
  https://www.ninds.nih.gov/Disorders/All-Disorders/Microcephaly-Information-Page
- National Institute of Neurological Disorders and Stroke: Seizures and Epilepsy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page
- National Institute on Deafness and Other Communication Disorders: Speech and Language Developmental Milestones
  https://www.nidcd.nih.gov/health/speech-and-language

Educational Resources

- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Disease InfoSearch: Rett syndrome, congenital variant
  http://www.diseaseinfosearch.org/Rett+syndrome%2C+congenital+variant/9249

- KidsHealth from Nemours: Delayed Speech or Language Development
  http://kidshealth.org/en/parents/not-talk.html
- MalaCards: foxg1 syndrome
  http://www.malacards.org/card/foxg1_syndrome

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities
  http://aaidd.org/
- Autism Society
  http://www.autism-society.org/
- International FOXG1 Foundation
  https://foxg1.com/
- Resource List from the University of Kansas Medical Center: Developmental Delay
  http://www.kumc.edu/gec/support/devdelay.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28foxg1+syndrome%5BTIAB%5D%29+OR+%28%28congenital%5BTIAB%5D%29+AND+%28Rett+syndrome%5BTIAB%5D%29+AND+%28FOXG1%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- RETT SYNDROME, CONGENITAL VARIANT
  http://omim.org/entry/613454

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214958/

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https://ghr.nlm.nih.gov/condition/foxg1-syndrome

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